Journal of the American College of Cardiology Vol. 45, No. 9, 2005

Published by Elsevier Inc.
ISSN 0735-1097/05/$30.00
doi:10.1016/j.jacc.2004.11.068

STATE-OF-THE-ART PAPER

Diets and Cardiovascular Disease

An Evidence-Based Assessment

Parin Parikh, BA,* Michael C. McDaniel, MD,† M. Dominique Ashen, PHD, CRNP,*
Joseph I. Miller, MD,† Matthew Sorrentino, MD, FACC,‡ Vicki Chan, BS,*
Roger S. Blumenthal, MD, FACC,* Laurence S. Sperling, MD, FACC*
Baltimore, Maryland; Atlanta, Georgia; and Chicago, Illinois

With rising obesity, despite low-fat diet recommendations, there is an increased interest in weight loss and alternative dietary approaches for cardiovascular health. Physicians must have an understanding of the literature to better counsel their patients about diets and cardiovascular disease. This review examines several dietary approaches to cardiovascular health and evaluates the available scientific evidence regarding these diets. (J Am Coll Cardiol 2005;45: 1379–87) © 2005 by the American College of Cardiology Foundation

Dietary advice regarding cardiovascular disease (CVD) prevention is complex. Much confusion stems from the lack of definitive data on available diets and their potential health benefits. For years, the American Heart Association (AHA) has recommended a low-fat diet of 55% of total calories from carbohydrates, 30% from fat, and 15% from protein, with cholesterol restricted to <300 mg/day (1). However, an unintended consequence of emphasizing this low-fat diet may have been to promote unrestricted carbohydrate intake (2).

The prevalence of obesity in America increased by 61% since 1991 (3). Each year, an estimated 300,000 U.S. adults die from obesity-related causes (4), and obesity plus physical inactivity account for approximately 9.4% of U.S. health care expenditures (5). Dietary improvement may significantly impact weight and cardiovascular morbidity. Due to the increasing prevalence of obesity, despite low-fat recommendations, many new popular diets have emerged. Although some of these new diets may offer health benefits, others may potentially harm cardiovascular or overall health. Physicians must have an understanding of these diets in order to counsel patients. The goal of this paper is to review several popular dietary approaches for cardiovascular health and evaluate the available scientific evidence behind these diets.

Low-carbohydrate diets. A low-carbohydrate diet was first characterized by William Banting in the 1860s (6), but this type of diet has currently received much attention due to *Dr. Atkins' New Diet Revolution* (7). The Atkins' Diet recommends two weeks of extreme carbohydrate restriction, followed by gradually increasing carbohydrates to 35 g/day. The Atkins' Diet has 68% of total calories from fat, 27% from protein, and 5% from carbohydrates (8). Other popular low-carbohydrate diets are summarized in Table 1.

Low-carbohydrate diets recommend limiting complex and simple sugars, causing the body to oxidize fat to meet energy requirements. During the initial carbohydrate restriction, the body resorts to ketosis for energy needs. Ketones are excreted in the urine with fluid. Rapid initial weight loss may be from this diuretic effect (8), which can be encouraging.

A drastic reduction in carbohydrates also leads to an overall decrease in caloric intake (9). Even when calories are not actively restricted, low-carbohydrate dieters consume fewer calories compared with baseline (10). Weight loss can be sustained by this reduction in caloric intake. Although palatable for the short term, low-carbohydrate diets raise several nutritional and cardiovascular concerns, as summarized in Table 2.

Four randomized, controlled clinical trials (Table 3) have compared low-carbohydrate diets with low-fat diets (11–15). Although the trials differed in design, all found an average of 4 to 6 kg greater weight loss in the low-carbohydrate group at six months. However, the two studies followed to one year showed no significant weight difference (11,12).

Foster et al. (11) conducted a randomized, controlled trial lasting one year. Sixty-three obese patients were assigned either a low-carbohydrate diet or a low-fat diet. The low-carbohydrate group showed greater weight loss at six months, but the weight loss between the groups was not significant at one year. Low-carbohydrate dieters showed a greater increase in high-density lipoprotein (HDL) cholesterol and a decrease in triglycerides that was independent of weight loss.

Stern et al. (12) conducted a one-year trial that followed 132 obese patients (body mass index ≥35 kg/m^2). The subjects were randomized to a carbohydrate-restricted or fat-restricted diet. Average caloric intake decreased by 510 kcal/day in the low-carbohydrate group, but only by 97

From the *Department of Medicine, Johns Hopkins Ciccarone Preventive Cardiology Center, Baltimore, Maryland; †Department of Medicine, Section of Preventive Cardiology, Emory University, Atlanta, Georgia; and the ‡University of Chicago, Department of Medicine, Section of Preventive Cardiology, Chicago, Illinois.

Manuscript received September 19, 2004; revised manuscript received November 23, 2004, accepted November 29, 2004.

JACC Vol. 45, No. 9, 2005
May 3, 2005:1379–87

Abbreviations and Acronyms

ALA = alpha-linolenic acid
CVD = cardiovascular disease
DASH = Dietary Approach to Stop Hypertension
DHA = docosahexaenoic acid
EPA = eicosapentaenoic acid
GI = glycemic index
GL = glycemic load
HDL = high-density lipoprotein
N3-FA = omega-3 polyunsaturated fatty acids
VLF = very low fat

kcal/day in the low-fat group ($p = 0.183$). At six months, the low-carbohydrate group showed greater weight loss, increased HDL cholesterol, decreased triglycerides, and increased insulin sensitivity. At one year, there was no difference in weight loss between the two groups, although those on the low-carbohydrate diet continued to have lower triglyceride and higher HDL cholesterol levels.

Brehm et al. (14) followed 53 female participants for six months in a randomized, controlled trial comparing a low-carbohydrate with a low-fat diet. Subjects met with a dietitian every other week and had group meetings twice a week. At six months, the low-carbohydrate group showed greater weight loss, increased HDL cholesterol, and decreased triglycerides.

Finally, Yancy et al. (15) conducted a six-month randomized, controlled trial of 120 overweight and hyperlipidemic patients. The intervention group followed a low-carbohydrate diet plus nutritional supplementation and received exercise recommendations, and the control group followed a low-fat diet. At six months, the low-carbohydrate group lost more weight than the low-fat group, and their estimated daily energy intake was 41 kcal lower. The low-carbohydrate group also had lower triglycerides and higher HDL cholesterol. However, this analysis is confounded by the nutritional supplements received by the intervention group, such as fish oils, which decrease triglyceride levels.

Bravata et al. (10) reviewed 94 low-carbohydrate diet studies. Weight loss in these studies was linked to caloric restriction, diet duration, and initial baseline weight and age. However, there was no association between weight loss and carbohydrate restriction, suggesting that short-term weight loss could instead be the result of caloric restriction and the ketosis-related diuretic effects. Of note, rapid, early weight loss, as well as the palatable nature of a low-carbohydrate diet, may act as motivating factors to remain on this type of diet (14).

Although there is no consensus on what appropriate attrition rates for clinical trials of diets should be, attrition rates of 24% to 39% (Table 4) point to the difficulty of following a low-carbohydrate diet over time. Only in one six-month trial (15) was the attrition rate in the low-carbohydrate group significantly lower ($p < 0.05$) than that in the low-fat group.

Table 1. Summary of Popular Low-Carbohydrate Diets*

The Atkins' Diet
68% fat, 27% protein, 5% carbohydrates
<35 g carbohydrate per day
Protein Power
54% fat, 26% protein, 16% carbohydrates
The Zone Diet
30% fat, 40% protein, 30% carbohydrates

*Listed are the contents of three popular low-carbohydrate diets. Adapted from data in reference 8.

Low-carbohydrate diets may increase HDL cholesterol, decrease triglyceride levels, and improve glycemic control, but there appears to be no significant difference in weight loss compared with a low-fat diet at one year. Because the longest trial extends to one year with relatively few subjects, more studies are required to assess the efficacy of a low-carbohydrate diet on long-term weight loss and cardiovascular outcomes.

Glycemic index diets. The glycemic index (GI) is a concept that has been used in diets such as the South Beach Diet (16), Sugar Busters (17), and the Zone Diet (18). These diets allow carbohydrate consumption as long as they have a low GI. The GI is a measure of the blood glucose response to intake of a particular carbohydrate (19). The higher the peak in postprandial blood glucose levels, the higher the GI value. The glycemic load (GL) is the product of dietary GI and total dietary carbohydrate, providing a useful measure of the total glycemic effect (20). Table 5 shows a list of common foods and their associated GI and GL. A high-GI diet has been proposed to increase hunger and elevate free fatty acid levels, leading to an increased risk of obesity, diabetes, and CVD (21). Several in vitro experiments indicate that elevated postprandial blood glucose levels cause oxidative stress, leading to endothelial damage and activation of coagulation (22).

The framework of the South Beach Diet includes an initial two-week period of extreme carbohydrate restriction followed by gradual re-introduction of low-GI carbohydrates. The maintenance phase encourages intake of fruits, vegetables, whole grains, mono- and polyunsaturated fats, omega-3 fatty acids, nuts, and moderate dairy products. Unlike the Atkins' Diet, the South Beach Diet encourages

Table 2. Low-Carbohydrate Diet Pros and Cons*

Pros	Cons
Initial weight loss	High-protein diet
Diuretic effect	Calcium balance
Palatable diet	Renal and hepatic complications
Easier to maintain	Potentially atherogenic
Caloric restriction	High in saturated fat and cholesterol
Reason for weight loss?	Low in fruits, vegetables, and whole grains

*This table summarizes the positive and negative aspects of low-carbohydrate diets. Adapted from data in references 7–10.

Table 3. Low-Carbohydrate Diet and Weight Loss*

	Foster et al. (11)	Stern et al. (12)	Brehm et al. (14)	Yancy et al. (15)
Length of trial	12 months	12 months	6 months	6 months
Low-CHO baseline weight (kg)	99 ± 20	130 ± 23	91 ± 8	97 ± 19
Low-CHO diet weight change (kg)	−4% ± 7%†	−5 ± 9†	−9 ± 1.0†	−12 ± 2†
Low-fat baseline weight (kg)	98 ± 16	132 ± 27	92 ± 6	98 ± 15
Low-fat diet weight change (kg)	−3% ± 6%†	−3 ± 8†	−4 ± 1.0†	−7 ± 2†
p Value (between groups)	0.26	0.195	<0.001	<0.001

*This table summarizes the four large randomized, controlled trials effects on weight loss and the duration of each trial. †$p < 0.05$ for difference from baseline within the group. Data are presented as the mean value ± SD. Adapted from data in references 11, 12, 14, and 15.
CHO = carbohydrate.

lean protein, such as fish and poultry, and allows olive oil as a source of mono- and polyunsaturated fat.

The longest interventional study conducted in humans related to GI was a crossover study lasting 12 weeks (23). Thirty women were randomized to a low-GI or high-GI diet. Those on a high-GI diet lost 7.4 kg, whereas those on a low-GI diet lost 9.4 kg ($p = 0.14$). In 16 women who participated in a 12-week follow-up, crossover study, those on a low-GI diet lost 7.4 kg, compared with 4.5 kg on a high-GI diet ($p < 0.05$). However, the results from other interventional studies, although shorter in duration and with smaller populations, have been inconsistent (24).

A possible association between a high-GI diet and diabetes has been observed. Studies that investigated this relationship include the Nurses' Health Study (25), which followed over 65,000 U.S. women for six years, the Health Professionals' Survey (26), which followed 42,750 U.S. men for six years, and the Iowa Women's Health Study, which followed 36,000 women for six years (27). All of these prospective cohort studies showed an association between diabetes and high GL. A recent meta-analysis of 14 randomized, controlled trials comparing low- and high-GI diets in diabetes management showed that glycated proteins were reduced 7.4% on a low-GI diet (28). Multiple cohort studies (Table 6) have been inconclusive as to whether a high-GI diet may also be linked to CVD risk factors (29–33).

High-GI diets may alter HDL metabolism. A survey of 1,420 British adults (32) evaluated GI through a seven-day diet survey and showed an inverse relationship between GI and HDL cholesterol. The Third National Health and Nutrition Examination Survey (NHANES III) (33), which followed 13,907 subjects older than 20 years old, demonstrated that for every 15-U increase in GI, there was a 0.06-mmol/l decrease in HDL cholesterol.

Many of these prospective cohort studies contain confounding variables. Most of these studies based their GI and GL calculations on self-reporting. Portion size and recall bias could result in inaccurate reporting (24). Also, the GI of a food can change depending on the method of food preparation and different types of the same food (i.e., different grains of rice). Despite suggestive evidence, no trials have shown that low-GI diets prevent CVD. Longer studies with more participants are needed before low-GI diets can be definitively recommended.

Very-low-fat (VLF) diets. Very-low-fat (VLF) diets allow less than 15% of total calories from fat (with an equal distribution of saturated, monounsaturated, and polyunsaturated fats), 15% from protein, and 70% from carbohydrates. The VLF diet includes variations of vegetarian diets that may include eggs and dairy. Although an AHA scientific statement concluded there were little long-term data to suggest that low-fat diets alone will sustain long-term weight loss, there is evidence that this diet can impact cardiovascular risk (34).

The Heidelberg trial (35) evaluated 113 patients with stable angina. The experimental group reduced fat to <20% of calories and total cholesterol to <200 mg/dl and engaged in moderate-intensity exercise. After 12 months, the intervention group's body weight decreased by 5% ($p < 0.001$), total cholesterol by 10% ($p < 0.001$), and triglycerides by 24% ($p < 0.001$). In the intervention group, progression of coronary lesions by angiography was decreased compared with that of controls ($p < 0.05$). However, given the confounding effects of exercise, this study makes it difficult to assess the effects of diet alone.

The Pritikin diet recommends <10% of calories from fat, 15% to 20% from protein, and the remainder from unrefined, complex carbohydrates. In a small three-week study combining statins, diet, and vigorous exercise, those on the Pritikin diet resulted in a further 19% reduction in total cholesterol. There was also an incremental benefit in low-density lipoprotein (LDL) cholesterol and triglycerides for

Table 4. Attrition Rates in Randomized, Controlled Trials*

Attrition Rate†	Foster et al. (11)	Stern et al. (12)	Brehm et al. (14)	Yancy et al. (15)
Low-carbohydrate diet	39% (12 months)	33% (12 months)	27% (6 months)	24%* (6 months)
Low-fat diet	43% (12 months)	47% (12 months)	52% (6 months)	43%* (6 months)

*This table summarizes the attrition rates for the low-carbohydrate and low-fat dieters in the four randomized, controlled trials investigating low-carbohydrate diets. †The attrition rate was significantly different between two groups ($p = 0.02$). Adapted from data in references 11, 12, 14, and 15.

Table 5. Glycemic Index and Glycemic Loads of Various Foods*

Food	Glycemic Index	Glycemic Load
Glucose	100	—
Cornflakes	92	24
Baked potato	85	26
Instant rice	75	28
White bread	70	10
Coca-cola	63	16
Wheat bread	52	10
Carrot	47	3
Spaghetti	41	20
Apple	40	6
Lentil beans	29	5
Peanuts	13	1

*This table shows the glycemic index and glycemic load of various foods compared with glucose. Adapted from data in reference 21.

those on the diet, but also a slight reduction in HDL cholesterol (36).

The Ornish Lifestyle Heart Trial (37) randomized 48 patients with moderate to severe coronary heart disease (CHD) to intensive life-style changes or usual care. The intensive life-style changes included a vegetarian diet with 7% of caloric intake coming from fat, moderate aerobic exercise, stress management training, smoking cessation, and group psychosocial support. A total of 195 coronary artery lesions were analyzed angiographically. Overall, 82% of experimental group patients had an average change toward lesion regression. At five years, there were 2.5 times fewer cardiac events in the intervention group, and the average percent diameter stenosis showed an 8% decrease in diameter, whereas the control group had 28% progression. However, the data are difficult to interpret due to the confounding effects of exercise, stress reduction, and 11-kg weight loss in the intervention group. Although the intervention seems beneficial, the small sample size and intense life-style changes raise concerns about the universal sustainability of such a program.

The VLF diet and intense life-style changes have significant results in terms of reducing risk factors and cardiac event rates. However, these studies are relatively small, and the programs involved may be influenced by selection bias. The programs require a motivated group of patients to undergo rigorous life-style adjustments. The VLF diet may be unnecessary if other life-style characteristics like exercise, smoking cessation, and stress management are optimized.

The Mediterranean Diet. The Mediterranean Diet is characterized by (38): 1) an abundance of plant food (fruit, vegetables, breads, cereals, potatoes, beans, nuts, and seeds); 2) minimally processed, seasonally fresh, locally grown foods; 3) desserts comprised typically of fresh fruit daily and occasional sweets containing refined sugars or honey; 4) olive oil (high in polyunsaturated fat) as the principal source of fat; 5) daily dairy products (mainly cheese and yogurt) in low to moderate amounts; 6) fish and poultry in low to moderate amounts; 7) up to four eggs weekly; 8) red meat rarely; and 9) and wine in low to moderate amounts with meals.

Although a Mediterranean-style diet has demonstrated greater weight reduction compared with control diets in randomized, controlled trials (39), the most impressive benefits of the diet are related to cardiovascular morbidity and mortality. No isolated aspect of the Mediterranean Diet explains these benefits, but much has focused on the omega-3 polyunsaturated fatty acids (N-3 FA). Examples of N-3 FA include eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) found in fatty fish like salmon, mackerel, herring, and trout (40). A form of N-3 FA derived from plants—alpha-linolenic acid (ALA)—is found in nuts, canola (rapeseed) oil, flaxseed, flaxseed oil, and soybean oil (40). Alpha-linolenic acid can be converted to EPA and DHA (41), which are thought be cardioprotective (41–46).

One major mechanism of protection may be related to the anti-arrhythmic effects of N-3 FA (47). Data from various animal, epidemiologic, and metabolic studies, as well as smaller clinical trials, demonstrate the benefits of N-3 FA in reducing the risk of sudden cardiac death (48). Omega-3 polyunsaturated fatty acids also decrease the arachidonic acid content of cell membranes, reduce eicosanoids, downregulate gene expression of adhesion molecules, and inhibit the synthesis of proinflammatory cytokines such as tumor necrosis factor-alpha, interleukin (IL)-1, and IL-2 (49). Moreover, fish oil supplements can lower triglycerides,

Table 6. Cohort Studies Investigating Low-Glycemic Index and Cardiovascular Disease Risk*

Cohort	Population	Intervention	Follow-Up	Results
Nurse's Health Study (29)	75,521 women	GL	10 yrs	GL directly associated with risk of CHD
Zutphen Elderly Study (30)	646 Dutch men	GI	10 yrs	GI showed no correlation to CHD, total cholesterol levels, HDL cholesterol, triglycerides
Italian case-control study (31)	881 Italians post-acute MI	GI and GL	4 yrs	No association between GL or GI with acute MI risk
British adult survey (32)	1,420 British adults	GI	Cross-sectional	Negative relation between GI of diet and serum HDL cholesterol
NHANES III (33)	13,907 U.S. adults	GI	Cross-sectional	Decrease of 0.06 mmol/l of HDL cholesterol for every 15-U increase in glycemic index

*This table summarizes the results of five large cohort studies investigating the glycemic index and glycemic load. Included are the length of each study, the number of participants, and the results. Adapted from data in references 29–33.

CHD = coronary heart disease; GI = glycemic index; GL = glycemic load; HDL = high-density lipoprotein; MI = myocardial infarction.

Table 7. Summary of Randomized, Controlled Trials With Mediterranean-Style Diets*

Study	Patients Enrolled	Follow-Up Time	Control Diet	Experimental Diet	Results
DART (55)	2,033 Post-MI men	2 yrs	No dietary advice	Fatty fish twice per week with goal of 500–800 mg/day of N-3 fatty acids	29% reduction in all-cause mortality, 27% decrease in fatal MI
Indian Experiment of Infarct Survival (53)	360 Post-acute MI	1 yr	Placebo	EPA supplement or ALA supplement	EPA: 50% decrease in cardiac death, 48% decrease in nonfatal MI ALA: 40% decrease in cardiac events
Lyon Diet Heart (56)	605 Post-MI	46 months	Prudent Western-style diet	Mediterranean diet rich in fish, fruits, vegetables, and ALA margarine	68% decrease in cardiac death and nonfatal MI; protective effects lasted >4 years
Indo-Mediterranean Diet (54)	1,000	2 yrs	Step I NCEP	Mediterranean style (fruits, grains, vegetables, mustard seed or soy bean oil, and walnuts)	Significant reduction in sudden cardiac death and nonfatal MI
GISSI-Prevenzione (57)	11,324 Post-MI	3.5 yrs	Placebo	1 g/day omega-3 fatty acid fish-oil supplements	20% decrease in mortality, 30% decrease in CV deaths, 46% decrease in sudden deaths

*This table summarizes five randomized, controlled trials investigating the Mediterranean-style diet. The table lists the number of patients randomized, the length of follow-up, the control diet in study, the experimental diet, and the results of the study. Adapted from data in references 53–57.

ALA = alpha-linolenic acid; CV = cardiovascular; EPA = eicosapentaenoic acid; MI = myocardial infarction; NCEP = National Cholesterol Education Program.

inhibit endothelial cell activation, and improve endothelial function in diabetics (50). They can also reduce platelet aggregation (51) and decrease the heart rate (52).

Multiple randomized, controlled trials have demonstrated the benefits of the Mediterranean Diet on secondary prevention of CVD (Table 7) (53–57). The Diet and Reinfarction Trial (DART) (49) followed 2,000 men for two years to study the effect on the secondary prevention of myocardial infarction (MI). The men were randomized to four groups. One group received advice in accordance with AHA dietary guidelines. Another group was advised to consume fish twice per week (300 g total) in order to achieve approximately 2.5 g of EPA weekly. A third group was told to increase cereal fiber intake to 18 g/day. A fourth group (controls) did not receive advice. In comparing the four groups, the fish group showed a 29% reduction in mortality compared with the control group. The rate of fatal MI was also less in the fish group.

The Lyon Diet Heart Study (56) randomized 605 participants with a previous MI for 46 months and showed an inverse relationship between ALA intake and the risk of a second MI. The intervention group was advised to eat more fish, fruits, and vegetables and to use an ALA-rich margarine. The control group was advised to follow a prudent diet. There was a 68% decrease in primary end points (cardiac death and nonfatal MI). Secondary end points (periprocedural infarctions, unstable angina, heart failure, stroke, and pulmonary or peripheral embolisms) also decreased. Of note, at four-year follow-up, most experimental patients were still closely following the recommended diet.

The largest randomized, controlled trial examining the benefits of fish oil supplements was the GISSI-Prevenzione trial (57), which followed 11,234 subjects for a mean of 42 months. Participants were randomized to four groups, with subjects receiving a placebo, fish oil supplements equivalent to 1 g of EPA/DHA per day, 300 mg of vitamin E per day, or both the fish oil supplements and vitamin E. The investigators found no effect of vitamin E on CVD. In the experimental group, there was an approximate 20% reduction over 3.5 years in cardiac death, nonfatal MI, and nonfatal stroke. The greatest benefit was seen in sudden cardiac death, with reductions of 35% to 45%.

Multiple prospective cohort studies (Table 8) support the benefit of a Mediterranean-style diet (58–60). Most recently, 22,043 patients from a Greek population completed a questionnaire for the European Prospective Investigation into Cancer and Nutrition (61). Investigators used a scale of 0 to 9 to estimate adherence to the Mediterranean Diet, with higher scores reflecting greater adherence. After a mean follow-up of 44 months, each two-point increment in adherence to the diet was associated with a 25% reduction in total mortality. Greater compliance was associated with reductions in CHD and cancer mortality. This study points to the possible synergistic effect of the Mediterranean Diet as a whole, rather than protective effects of any one aspect.

There is consistent basic science and clinical trial evidence for the cardioprotective effects of the Mediterranean Diet, particularly in secondary prevention of acute and fatal MI. Patients on a Mediterranean diet have been shown to lose more weight, have lower C-reactive protein levels, have less insulin resistance, have lower total cholesterol and triglyceride and higher HDL levels, and have a decreased prevalence of the metabolic syndrome (39). Although attrition data are not available for all the trials, the Lyon Diet Heart trial concluded most experimental patients were still closely following the recommended diet at four years (56). The AHA guidelines recommend consuming 1 g/day of EPA/DHA; however, it is quite difficult to sustain this level with

JACC Vol. 45, No. 9, 2005
May 3, 2005:1379–87

Table 8. Large Prospective Cohort Studies Investigating the Mediterranean Diet*

Cohort	Population	Intervention	Follow-Up	Results
Nurse's Health Study (58)	84,688 women	Fish and N3-FA consumption	16 yrs	High consumption of fish (five times a week) cuts the risk of dying from CHD by 45%, compared with women who rarely ate fish
Physicians' Health Study (59)	20,551 men	Blood levels of N3-FA	17 yrs	Relative risk of sudden death lower among men with higher blood levels of N3-FA
Cardiovascular Health Study (60)	5,201 ≥65 years old	Plasma N3-FA	7 yrs	Higher concentration of EPA, DHA, or ALA associated with lower risk of fatal ischemic heart disease
European Prospective Investigation into Cancer and Nutrition (61)	22,043 Greeks	Mediterranean Diet scale	44 months	Two-point increase in adherence with Mediterranean Diet associated with 25% reduction in total mortality

*This table summarizes the results of four large cohort studies examining the Mediterranean Diet. Included are the number of participants in the study, the intervention, the follow-up, and the results. Adapted from data in references 58–61.

DHA = docosahexaenoic acid; N3-FA = omega-3 polyunsaturated fatty acids; other abbreviations as in Tables 6 and 7.

fish consumption alone (40). Based on the GISSI trial, the AHA and others (62) have therefore recommended taking supplements of three 1-g fish oil capsules per day.

In regard to primary prevention, studies show that a Mediterranean diet may be linked to decreased rates of sudden cardiac death, CHD, and possibly overall mortality. A systematic review by Hu and Willet (52) of metabolic, epidemiologic, and clinical trial evidence indicated that three dietary strategies are effective in preventing CHD: 1) substituting non-hydrogenated unsaturated fats for saturated and trans-fats; 2) increasing consumption of omega-3 fatty acids; and 3) consuming more fruits, vegetables, nuts, and whole grains, while avoiding refined grain products.

There are some concerns regarding the Mediterranean Diet. Potential side effects of the diet include a fishy aftertaste, gastrointestinal discomfort, and possibly an increase in LDL cholesterol (40). Another concern is mercury exposure. In fact, the Food and Drug Administration (FDA) currently recommends that children and women who are pregnant and/or lactating should avoid fish consumption (40).

Dietary Approaches to Stop Hypertension (DASH). The DASH Diet is similar to a Mediterranean-type diet, emphasizing high intake of fruits, vegetables, low-fat dairy products, whole grains, nuts, fish, and poultry, as well as reducing total and saturated fats. Reduced intake of red meat, sweets, and sugar-containing beverages is encouraged, which results in a diet high in potassium, calcium, magnesium, and fiber. This dietary approach has been shown to lower blood pressure, but little has been published regarding weight loss.

The original DASH trial (63) consisted of 459 subjects with systolic blood pressures <160 mm Hg and diastolic blood pressures between 80 and 95 mm Hg. For three weeks, all participants were fed a control diet low in fruits, vegetables, and dairy products, and with a fat content typical of an American diet (37% of daily caloric intake). During the following eight weeks, the participants were randomized to one of three diets: the control diet, a diet rich in fruits and vegetables, or the DASH Diet.

The DASH Diet reduced systolic blood pressure by 5.5 mm Hg and diastolic blood pressure by 3.3 mm Hg, as compared with controls. Subgroup analysis showed that African Americans and those with hypertension had the greatest reduction in blood pressure. The DASH diet results might be applied to a larger group due to the heterogeneous population: half of the participants were women, 60% were African American, and 37% had household incomes of <$30,000 per year. One limitation of applying the DASH Diet to the general population is that the study was carried out in a very controlled setting, where all the meals were prepared for the subjects, and thus no comments may be made regarding attrition rates for the diet.

The DASH Diet was not low in sodium, but still reduced blood pressure. A meta-analysis of 56 randomized, controlled trials that included over 3,500 participants did not support universal sodium restriction, but instead only recommended dietary sodium restriction in the elderly (64).

To further investigate the effects of sodium restriction, the DASH-Sodium Trial (65) was conducted. A total of 412 subjects were randomized to the control diet or DASH diet for 90 days. Within each arm, patients were further stratified and assigned to three diets: high (3.5 g/day), intermediate (2.3 g/day), or low (1.2 g/day) sodium, each for a 30-day period in a random order. In the control group, there was a dose response with the greater reductions in sodium intake correlating with greater decreases in blood pressure. For those on the DASH Diet, the dose response persisted, although the effects of sodium reduction were smaller. Additionally, there was no significant difference between high and intermediate sodium intake on diastolic blood pressure for those on the DASH Diet. The difference was only significant between the high- and low-sodium groups. The DASH Diet can reduce systolic blood pressure by 5.5 mm Hg and diastolic blood pressure by 3.3 mm Hg. However, the effect of sodium reduction on hypertension remains controversial. Lowering sodium to the levels of 1.2 g/day, as achieved in the lowest sodium intake group of the DASH-Sodium Trial, would be nearly impossible without changes in the food industry, as 75% of sodium intake comes from additions made in processing (66).

Table 9. Diet Summary Points

Low-Carbohydrate Diet
Short-term weight loss
Long-term effects on CVD unknown
Guide to initiate decreased energy intake
Glycemic Index and Diet
Unproven effects on CVD
Guide to decreased consumption of energy-dense carbohydrates and initiate weight loss
Very-Low-Fat Diet
Possible decrease in cardiac events
Concerns about universal applicability and sustainability
Mediterranean Diet
Secondary prevention
Prevention of sudden cardiac death
Healthy overall approach to dieting
Long-term sustainability
DASH
Decreased hypertension
Similar to Mediterranean Diet

CVD = cardiovascular disease.

Conclusions. Physicians and patients are continually searching for optimal methods to lose weight and maintain a diet that sustains cardiovascular health. Patient frustration with current AHA and National Cholesterol Education Program (NCEP) low-fat guidelines has been evident by poor compliance to these recommended diets and the increasing prevalence of obesity. The scientific community has also begun to question the low-fat diet–heart hypothesis (67). A few summary points (Table 9) can be extracted from this review.

A low-carbohydrate diet can lead to short-term weight loss. However, the long-term effects on CHD risk factors, such as weight loss, HDL and LDL cholesterol, triglycerides, glycemic control, and blood pressure, are unknown.

Moderate-sized studies on VLF diets show decreases in cardiovascular events, but the sustainability and applicability of these diets to a large population is a concern. Moreover, as many of these studies also included life-style changes as part of the treatment, it is not possible to separate these effects from those of the diet itself.

No adequate randomized, controlled trials have evaluated the effects of a low-GI diet on CVD. Nonetheless, diets based on a low GI, such as the South Beach Diet, can encourage consumption of mono- and polyunsaturated fats, lean protein, fruits, vegetables, and whole-grain foods instead of simple, refined carbohydrates.

The Mediterranean Diet has been shown to be cardioprotective in both prevention of sudden cardiac death and secondary prevention.

The DASH Diet, which has shown to reduce blood pressure, fits well into the framework of a Mediterranean Diet and can help decrease the cardiovascular risk of hypertension.

Although none of the reviewed diets are independently perfect for weight loss and cardiovascular health, an optimal diet can be extracted from this review. Specifically, such a diet would encourage: 1) decreased carbohydrate intake, especially of refined and high-GI carbohydrates; 2) increased consumption of fruits, vegetables, and whole grains;

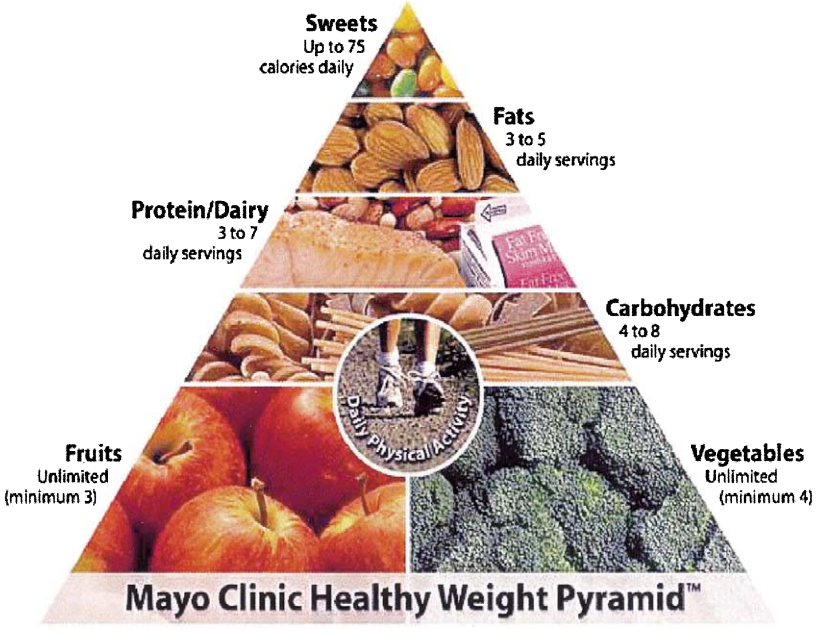

Figure 1. The Mayo Clinic Healthy Weight Pyramid is a tool to help lose weight or maintain weight. The pyramid offers a somewhat different approach to healthy eating compared with the USDA Food Guide Pyramid. It focuses on low energy-dense foods, which have a small number of calories in a large amount of food. The foundation of the pyramid is unlimited amounts of vegetables and fruits (minimum four servings per day). One serving of vegetables equals 25 calories; one serving of fruit equals 60 calories. Level two in the pyramid is carbohydrates, including whole grains (four to eight servings per day). One serving of carbohydrate equals 70 calories. Protein/dairy is the third level of the pyramid (three to seven servings per day). One serving equals 70 calories. Fats, the fourth level of the pyramid, include heart-healthy olive oil, nuts, canola oil, and avocados (three to five servings per day). One serving of fat equals 45 calories.

3) increased intake of polyunsaturated fats by increasing consumption of plant oils and fish; 4) and moderate intake of low-fat dairy products and nuts.

Although many patients desire quick weight loss, patients should understand the basic concept that food is fuel, and people will lose weight if they burn more calories than they consume. Just as patients should not restrict fat and eat unrestricted amounts of carbohydrates, patients should not decrease carbohydrates and eat unrestricted amounts of fat. Portion size and total caloric intake is often more important than individual foods.

In place of the traditional USDA food pyramid, the Mayo Clinic has published an alternative healthy weight food pyramid (Fig. 1) (68). This pyramid illustrates an updated version of a properly balanced diet and promotes a healthy and sustainable dietary change instead of relying on short-term diets (69), recommendations supported by the evidence presented in this review. By encouraging patients to adopt an active lifestyle and to lose weight gradually using an evidence-based dietary approach, physicians can better counsel patients toward improved cardiovascular health.

Reprint requests and correspondence: Dr. Laurence Sperling, The Emory Clinic, 1525 Clifton Road, Suite 214, Atlanta, Georgia 30322. E-mail: Laurence_Sperling@emoryhealthcare.org.

REFERENCES

1. Krauss RM, Eckel RH, Howard B, et al. AHA dietary guidelines, revision 2000: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association. Circulation 2000;102:2296–311.
2. Weinber SL. The diet-heart hypothesis: a critique. J Am Coll Cardiol 2004;43:731–3.
3. Mokdad AH, Bowman BA, Ford ES, et al. The continuing epidemics of obesity and diabetes in the United States. JAMA 2001;286:1195–200.
4. Allison D, Fontaine K, Manson J, Stevens J, VanItallie T. Annual deaths attributable to obesity in the United States. JAMA 1999;282:1530–8.
5. Colditz G. Economic costs of obesity and inactivity. Med Sci Sports Exerc 1999;31 Suppl 11:S663–7.
6. Banting W. Letter on Corpulence, Addressed to the Public. 2nd edition. London: Harisson and Sons, 1863.
7. Atkins RC. Dr. Atkins' New Diet Revolution. New York, NY: Avon Books, 1998.
8. St. Jeor ST, Howard BV, Prewitt TE, et al. Dietary protein and weight reduction: a statement for healthcare professionals from the Nutrition Committee of the Council on Nutrition, Physical Activity, and Metabolism of the American Heart Association. Circulation 2001;104:1869–74
9. Bonow RO, Eckel RH. Diet, obesity, and cardiovascular risk. N Engl J Med 2003;348:2057–8.
10. Bravata DM, Sander L, Huang J, et al. Efficacy and safety of low-carbohydrate diets: a systematic review. JAMA 2003;289:1837–50.
11. Foster GD, Wyatt HR, Hill JO, et al. A randomized trial of a low-carbohydrate diet for obesity. N Engl J Med 2003;348:2082–90.
12. Stern L, Iqbal N, Seshadri P, et al. The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial. Ann Intern Med 2004;140:778–85.
13. Samaha FF, Iqbal N, Seshadri P, et al. A low-carbohydrate as compared with a low-fat diet in severe obesity. N Engl J Med 2003;348:2074–81.
14. Brehm BJ, Seeley RJ, Daniels SR, D'Alessio DA. A randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. J Clin Endocrinol Metab 2003;88:1617–23.
15. Yancy WS, Olsen MK, Guyton JR, et al. A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia. Ann Intern Med 2004;140:769–77.
16. Agatston A. The South Beach Diet: The Delicious, Doctor-Designed, Foolproof Plan for Fast and Healthy Weight Loss. New York, NY: Rodale, 2003.
17. Sugar Busters! Concept. Available at: http://www.sugarbusters.com/filessb/concept.html. Accessed May 11, 2004.
18. ZonePerfect Nutrition Program. Available at: http://www.zoneperfect.com/site/content/guide_02_ZoneDiet.asp. Accessed May 11, 2004.
19. Jenkins DJA, Thomas DM, Wolever S, et al. Glycemic index of food: a physiological basis for carbohydrate exchange. Am J Clin Nutr 1981;34:362–6.
20. Jenkins DJA, Kendall CWC, Augustin LSA, et al. Glycemic index: overview of implications in health and disease. Am J Clin Nutr 2002;76:266S–73S.
21. Foster-Powell K, Holt SHA, Brand-Miller JC. International table of glycemic index and glycemic load values: 2002. Am J Clin Nutr 2002;76:5–56.
22. Lefebvre PJ, Scheen AJ. The postprandial state and risk of cardiovascular disease. Diabet Med 1998;15:S63–8.
23. Slabber M, Barnard HC, Kuyl JM, Dannhauser A, Schall R. Effects of a low-insulin-response, energy-restricted diet on weight loss and plasma insulin concentrations in hyperinsulinemic obese females. Am J Clin Nutr 1994;60:48–53.
24. Pi-Sunyer FX. Glycemic index and disease. Am J Clin Nutr 2002;76:290S–98S.
25. Salmeron J, Manson JE, Stampfer MJ, et al. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. JAMA 1997;277:472–7.
26. Salmeron J, Ascherio A, Rimm EB, et al. Dietary fiber, glycemic load, an risk of NIDDM in men. Diabetes Care 1997;20:545–50.
27. Meyer KA, Kushi LH, Jacobs DR, Slavin J, Sellers TA, Folsom AR. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. Am J Clin Nutr 2000;71:921–30.
28. Brand-Miller J, Hayne S, Petocz P, Colagiuri S. Low-glycemic index diets in the management of diabetes: a meta-analysis of randomized controlled trials. Diabetes Care 2003;26:2261–7.
29. Liu S, Willett WC, Stampfer MJ, et al. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in U.S. women. Am J Clin Nutr 2000;71:1455–61.
30. van Dam RM, Visscher AW, Feskens EJ, Verhoef P. Kromhout D. Dietary glycemic index in relation to metabolic risk factors and incidence of coronary heart disease: the Zutphen Elderly Study. Eur J Clin Nutr 2000;54:726–31.
31. Tavani A, Bosetti C, Negri E, Augustin LS, Jenkins DJA. La Vecchia C. Carbohydrates, dietary glycaemic load and glycaemic index, and risk of acute myocardial infarction. Heart 2003;89:722–6.
32. Frost G, Leeds AA, Doré CJ, Madeiros S, Brading S, Dornhorst A. Glycaemic index as a determinant of serum HDL-cholesterol concentration. Lancet 1999;353:1045–8.
33. Ford ES, Liu S. Glycemic index and serum high-density lipoprotein cholesterol concentration among U.S. adults. Arch Intern Med 2001;161:572–6.
34. Lichtenstein AH, Van Horn L. AHA science advisory: very low fat diets. Circulation 1998;98:935–9.
35. Niebauer J, Hambrecht R, Marburger C, et al. Impact of intensive physical exercise and low-fat diet on collateral vessel formation in stable angina pectoris and angiographically confirmed coronary artery disease. Am J Cardiol 1995;76:771–5.
36. Barnard RJ, DiLauro SC, Inkeles SB. Effects of intensive diet and exercise intervention in patients taking cholesterol-lowering drugs. Am J Cardiol 1997;79:1112–4.
37. Ornish D, Scherwitz LW, Billings JH. Intensive lifestyle changes for reversal of coronary heart disease. JAMA 1998;280:2001–7.
38. Hu FB. The Mediterranean Diet and mortality—olive oil and beyond. N Engl J Med 2003;348:2595–6.
39. Esposito K, Marfella R, Ciotola M, et al. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome. JAMA 2004 ;292:1440–6.

40. Kris-Etherton PM, Harris WS, Appel LJ, et al. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Circulation 2002;106:2747–57.
41. Grundy SM. N-3 fatty acids: priority for post-myocardial infarction clinical trials. Circulation 2003;107:1834–6.
42. Das UN. Beneficial effect(s) of n-3 fatty acids in cardiovascular disease: but why and how? Prostaglandins Leukot Essent Fatty Acids 2001; 63:351–62.
43. Calder PC, Grimble RF. Polyunsaturated fatty acids, inflammation and immunity. Eur J Clin Nutr 2002;56 Suppl 3:S14–9.
44. Leaf A. The electrophysiologic basis for the anti-arrhythmic and anticonvulsant effects of n-3 polyunsaturated fatty acids: heart and brain. Lipids 2001;36 Suppl:S107–10.
45. Schoene NW. Vitamin E and omega-3 fatty acids: effectors of platelet responsiveness. Nutrition 2001;17:793–6.
46. Mori TA, Beilin LJ. Long-chain omega-3 fatty acids, blood lipids and cardiovascular risk reductions. Curr Opin Lipidol 2001;12:11–7.
47. Leaf A, Kang JX, Xiao Y, Billman GE. Clinical prevention of sudden cardiac death by n-3 polyunsaturated fatty acids and mechanism of prevention of arrhythmias by n-3 fish oils. Circulation 2003;107: 2626–52.
48. Kang JX, Leaf A. Prevention of fatal cardiac arrhythmias by polyunsaturated fatty acids. Am J Clin Nutr 2000;71:202S–7S.
49. von Shacky C. N-3 fatty acids and prevention of coronary atherosclerosis. Am J Clin Nutr 2000;71:224S–7S.
50. Brown A, Hu FB. Dietary modulation of endothelial function. Am J Clin Nutr 2001;73:673–86.
51. Dallongeville J, Yarnell J, Ducimetiere P, et al. Fish consumption is associated with lower heart rates. Circulation 2003;108:820–5.
52. Hu FB, Willett WC. Optimal diets for prevention of coronary heart disease. JAMA 2002;288:2569–78.
53. Singh RB, Niaz MA, Sharma JP, Kumar R, Rastogi V, Moshiri M. Randomized, double-blind, placebo-controlled trial of fish oil and mustard oil in patients with suspected acute myocardial infarction: the Indian Experiment of Infarct Survival-4. Cardiovas Drugs Ther 1997;11:485–91.
54. Singh RB, Dubnov G, Niaz MA, et al. Effect of an Indo-Mediterranean diet on progression of coronary artery disease in high risk patients (Indo-Mediterranean Diet Heart Study): a randomized single-blind trial. Lancet 2002;360:1455–61.
55. Burr ML, Gilbert JH, Holliday RM, et al. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: Diet and Reinfarction Trial (DART). Lancet 1989;2:757–61.
56. de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean Diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. Circulation 1999;99:779–85.
57. The GISSI-Prevenzione Investigators. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Lancet 1999;354:447–55.
58. Hu FB, Bronner L, Willett WC, et al. Fish and omega-3 fatty acid intake and risk of coronary heart disease in women. JAMA 2002;287: 1815–21.
59. Albert CM, Campos H, Stampfer MJ, et al. Blood levels of long-chain n-3 fatty acids and the risk of sudden death. N Engl J Med 2002;346:1113–8.
60. Lemaitre RN, King IB, Mozaffarian D, et al. n-3 Polyunsaturated fatty acids, fatal ischemic heart disease, and nonfatal myocardial infarction in older adults: the Cardiovascular Health Study. Am J Clin Nutr 2003;77:319–25.
61. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean Diet and survival in a Greek population. N Engl J Med 2003;348:2599–608.
62. Harris WS. N-3 long-chain polyunsaturated fatty acids reduce risk of coronary heart disease death: extending evidence to the elderly. Am J Clin Nutr 2003;77:279–80.
63. Appel LJ, Moore TJ, Obarzenek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. N Engl J Med 1997;336:1117–24.
64. Midgley JP, Matthew AG, Greenwood CM, Logan AG. Effect of reduced dietary sodium on blood pressure: a meta-analysis of randomized controlled trials. JAMA 1996;275:1590–7.
65. Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) Diet. N Engl J Med 2001;344:3–10.
66. Whelton PK, He J, Appel LJ, et al. Primary prevention of hypertension: clinical and public health advisory from the National High Blood Pressure Program. JAMA 2002;288:1882–8.
67. Weinberg SL. The Diet-Heart Hypothesis: a critique. J Am Coll Cardiol 2004;43:731–3.
68. Mayo Clinic Healthy Weight Pyramid. Available at: http://www.mayoclinic.org/news2000-av/pyramid.jpg. Accessed May 11, 2004.
69. Willett WC. Reduced-carbohydrate diets: no roll in weight management? Ann Intern Med 2004;140:836–7.